GENETIC CHARACTERIZATION OF THE *mar* LOCUS AND PRELIMINARY IDENTIFICATION OF MarA TARGET GENES.

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The *mar* locus of *Escherichia coli* controls the intrinsic level of resistance to a variety of structurally unrelated antibiotics. Constitutive expression of *marA* or loss of function mutations in *marR* result in antibiotic resistance. These genes are organized in an operon of the structure *marRAB*, and transcription of this locus is inducible by the weak acid sodium salicylate. Moreover, a low copy number plasmid containing only the *marRA* genes under the control of the *mar* promoter is sufficient to restore salycilate-inducible antibiotic resistance to a strain containing a deletion of the *mar* region of the chromosome. Protein fusions of *lacZ* to *marR* and *marA* have been constructed to study the regulation of *mar* gene expression, and the results confirm the idea that *marR* encodes a repressor of *marRAB* expression.

In order to identify genes whose products couple the presence of salycilate with the inactivation of MarR, a genetic screen was devised. Mutants that were defective simultaneously in salicylate induction of *marA-lacZ* fusion enzyme expression and antibiotic resistance were sought. Four such mutants have been isolated and found to map outside of the *mar* locus, and are thus genetic candidates for components of a *mar*-related sensor mechanism.

An inducible *marA* expression system has also been constructed and used to study the kinetics of the antibiotic resistance response as well as to identify *marA* target genes, using two dimensional gel electrophoresis. These studies should help to clarify the mechanisms by which *mar* gene expression is regulated to affect the level of antibiotic accumulation in this organism.

Source: https://www.industrydocuments.ucsf.edu/docs/khmv0000